IN THE CLAIMS:

This listing of claims will replace all prior versions, and listing, of claims in the application.

Listing of the Claims:

1. (Previously presented) A method of measurement of mitotic activity from histopathological specimen image data, the method comprising the steps of:
    a) identifying pixels in the image data having luminances associated with mitotic figures;
    b) selecting from among the identified pixels a reference pixel which is sufficiently close in position and luminance to another identified pixel to provide a reference colour;
    c) locating pixels in the image data with luminances sufficiently close to that of the reference colour to indicate potentially mitotic figures;
    d) incrementing image regions corresponding to potentially mitotic figures from the located pixels by adding pixels thereto, potential increments to image regions being implemented or rejected by according to whether or not their luminances are sufficiently close to respective image region luminances and sufficiently far from an image data background luminance;
    e) selecting grown image regions on the basis of thresholds for image region area, compactness and width/height ratio; and
    f) counting selected grown image regions as actually indicating mitotic figures on the basis of thresholds for number of such regions.

2. (Previously presented) A method according to Claim 1 wherein the step of selecting grown image regions also involves thresholds for ratio of image region luminance to background luminance and area difference between areas derived by growing each image region with multiple thresholds.

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3.   (Previously presented) A method according to Claim 2 wherein the thresholds for image region area, compactness, width/height ratio, luminance and area difference are: 355 pixels < area < 1700 pixels, 0.17 < compactness < 0.77, width/height ratio < 2.7, luminance percentage < 44%, area difference < 23area/100.

4.   (Previously presented) A method according to Claim 1 wherein the step of counting selected grown image regions as actually indicating mitotic figures also involves thresholds for region area and luminance.

5.   (Previously presented) A method according to Claim 1 wherein successive potential increments to image regions are individual pixels each of which is an immediate row or column neighbor of an existing image region pixel.

6.   (Previously presented) A method according to Claim 1 wherein step b) is implemented with a reference pixel having a luminance differing by less than 8% compared to another identified pixel distant from it by not more than two percent of a smaller of two image dimensions.

7.   (Previously presented) A method according to Claim 1 wherein step a) includes white balancing and median filtering the image data prior to identifying pixels having luminances corresponding to mitotic figures.

8.   (Previously presented) A method according to Claim 1 wherein in step c) pixels are cued for acceptance or rejection as regards indicating mitotic figures by:
   a)   thresholding colour image data to remove pixels lacking intensities associated with mitotic figure imagery,
   b)   removal pixels not present in all colors, and
   c)   thresholding image region areas to remove those too small and too large to be potential mitotic figures.

9.   (Previously presented) A method according to Claim 1 wherein in step c) pixels

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are cued for acceptance or rejection as regards indicating mitotic figures by:

a)   segmenting to identify pixels with intensities associated with mitotic figure imagery,

b)   thresholding image region areas to remove those too small and too large to be potential mitotic figures,

c)   cluster analysis to determine whether or not a pixel's image region is in a sufficiently large cluster, and

d)   necrotic and hairy edge filtering.

10.   (Currently amended) A method of measuring mitotic activity from histopathological specimen color image data, the method having the steps of:

a)   staining a histopathological specimen with a staining agent to <u>color and</u> delineate tissue and cellular structure appropriately for assessment of mitotic activity,

b)   obtaining <u>color</u> image data from <u>the staining of</u> the stained histopathological specimen,

c)   measuring an intensity profile of an image region <u>in the color image data, the image region</u> corresponding to a potentially mitotic figure, <s>and</s>

d)   counting the image region as indicating a mitotic figure if its <u>intensity</u> profile has a <s>value</s> <u>non-zero number of pixels with intensity associated with mitotic figure imagery, and that pixel number is</u> greater than a prearranged threshold <u>value,</u> <s>at a position in the profile having intensity associated with mitotic figure imagery.</s>

e)   <u>if one or more other image regions corresponding to potentially mitotic figures are available in the specimen image, repeating steps c) and d) for such region or regions,</u>

f)   <u>repeating steps c), d) and e) for additional histopathological specimen image data in order to obtain mitotic figure counts for a plurality of specimen images, and</u>

g)   <u>summing the mitotic figure counts obtained in steps c) to f) to provide an indication of degree of mitotic activity.</u>

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11. (Previously presented) A method of measuring mitotic activity from histopathological specimen image data, the method having the steps of:

a) measuring an intensity profile of an image region corresponding to a potentially mitotic figure, and

b) counting the image region as indicating a mitotic figure if its profile has a first value not greater than the prearranged threshold at a position in the profile having intensity associated with mitotic figure imagery, a second value greater than a prearranged second threshold, a third value greater than a prearranged third threshold, and a minimum value less than a prearranged fourth threshold.

12. (Previously presented) A method according to Claim 11 wherein the first value is at one end of the profile, the first and second values adjoin one another in the profile and the third value does not adjoin the second value.

13. (Previously presented) A method according to Claim 11 wherein the image data comprise a first Principal Component obtained by Principal Component Analysis (PCA) of colored image data.

14. (Previously presented) A method according to Claim 11 wherein step a) includes preprocessing image data by:

i) decomposing the image data into overlapping sub-images,

ii) applying PCA to the sub-images to derive a first Principal Component image,

iii) thresholding the first Principal Component image to produce a binary image of blobs and background

iv) rejecting blobs adjacent to or intersecting sub-image boundaries,

v) filling holes in blobs,

vi) rejecting blobs too small to correspond to potential mitotic figures, and

vii) reassembling the sub-images into a single image for image region profile measurement as aforesaid in step a).

15. (Previously presented) A method according to Claim 14 wherein after step g) pixels are cued for acceptance or rejection as regards indicating mitotic figures by:

a) thresholding colour image data to remove pixels lacking intensities associated with mitotic figure imagery,

b) removal pixels not present in all colors, and

c) thresholding image region areas to remove those too small and too large to be potential mitotic figures.

16. (Previously presented) A method according to Claim 14 wherein after step g) pixels are cued for acceptance or rejection as regards indicating mitotic figures by:

a) segmenting to identify pixels with intensities associated with mitotic figure imagery,

b) thresholding image region areas to remove those too small and too large to be potential mitotic figures,

c) cluster analysis to determine whether or not a pixel's image region is in a sufficiently large cluster, and

d) necrotic and hairy edge filtering.

17. (Previously presented) Computer apparatus for measuring mitotic activity from histopathological specimen image data, the apparatus being programmed to execute the steps of:

a) identifying pixels in the image data having luminances associated with mitotic figures;

b) selecting from among the identified pixels a reference pixel which is sufficiently close in position and luminance to another identified pixel to provide a reference colour;

c) locating pixels in the image data with luminances sufficiently close to that of the reference colour to indicate potentially mitotic figures;

d) incrementing image regions corresponding to potentially mitotic figures

from the located pixels by adding pixels thereto, potential increments to image regions being implemented or rejected by according to whether or not their luminances are sufficiently close to respective image region luminances and sufficiently far from an image data background luminance;

e) selecting grown image regions on the basis of thresholds for image region area, compactness and width/height ratio; and

f) counting selected grown image regions as actually indicating mitotic figures on the basis of thresholds for number of such regions.

18. (Previously presented) Computer apparatus according to Claim 17 programmed to execute the step of selecting grown image regions by also using thresholds for ratio of image region luminance to background luminance and area difference between areas derived by growing each image region with multiple thresholds.

19. (Previously presented) Computer apparatus according to Claim 18 wherein the thresholds for image region area, compactness, width/height ratio, luminance and area difference are: 355 pixels < area < 1700 pixels, 0.17 < compactness < 0.77, width/height ratio < 2.7, luminance percentage < 44%, area difference < 23area/100.

20. (Previously presented) Computer apparatus according to Claim 17 programmed to execute the step of counting selected grown image regions as actually indicating mitotic figures by also using thresholds for region area and luminance.

21. (Previously presented) Computer apparatus according to Claim 17 wherein successive potential increments to image regions are individual pixels each of which is an immediate row or column neighbor of an existing image region pixel.

22. (Previously presented) Computer apparatus according to Claim 17 programmed to execute step b) with a reference pixel having a luminance differing by less than 8% compared to another identified pixel distant from it by not more than two

percent of a smaller of two image dimensions.

23. (Currently amended) Computer apparatus for measuring mitotic activity from histopathological specimen color image data obtained from a histopathological specimen stained with a staining agent to color and delineate tissue and cellular structure appropriately for assessment of mitotic activity, the apparatus being programmed to execute the steps of:

a) measuring an intensity profile of an image region in the color image data, the image region corresponding to a potentially mitotic figure, and

b) counting the image region as indicating a mitotic figure if its intensity profile has a ~~value~~ non-zero number of pixels with intensity associated with mitotic figure imagery, and that pixel number is greater than a prearranged threshold value, ~~at a position in the profile having intensity associated with mitotic figure imagery.~~

c) if one or more other image regions corresponding to potentially mitotic figures are available in the specimen image, repeating steps a) and b) for such region or regions,

d) repeating steps a), b) and c) for additional histopathological specimen image data in order to obtain mitotic figure counts for a plurality of specimen images, and

e) summing the mitotic figure counts obtained in steps a) to d) to provide an indication of degree of mitotic activity.

24. (Previously presented) Computer apparatus for measuring mitotic activity from histopathological specimen image data, the apparatus being programmed to execute the steps of:

a) measuring an intensity profile of an image region corresponding to a potentially mitotic figure, and

b) counting an image region as indicating a mitotic figure if its profile has a first value not greater than the prearranged threshold at a position in the profile having intensity associated with mitotic figure imagery, a second value greater than a prearranged second threshold, a third value greater

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than a prearranged third threshold, and a minimum value less than a prearranged fourth threshold.

25. (Previously presented) Apparatus according to Claim 24 wherein the first value is at one end of the profile, the first and second values adjoin one another in the profile and the third value does not adjoin the second value.

26. (Previously presented) Apparatus according to Claim 24 wherein the image data comprise a first Principal Component obtained by Principal Component Analysis (PCA) of colored image data.

27. (Previously presented) A computer software product comprising a computer readable medium encoded with computer readable instructions and for use in measuring mitotic activity from histopathological specimen image data, the computer readable instructions being for controlling computer apparatus to implement the steps of:

a) identifying pixels in the image data having luminances associated with mitotic figures;

b) selecting from among the identified pixels a reference pixel which is sufficiently close in position and luminance to another identified pixel to provide a reference colour;

c) locating pixels in the image data with luminances sufficiently close to that of the reference colour to indicate potentially mitotic figures;

d) incrementing image regions corresponding to potentially mitotic figures from the located pixels by adding pixels thereto, potential increments to image regions being implemented or rejected by according to whether or not their luminances are sufficiently close to respective image region luminances and sufficiently far from an image data background luminance;

e) selecting grown image regions on the basis of thresholds for image region area, compactness and width/height ratio; and

f) counting selected grown image regions as actually indicating mitotic

figures on the basis of thresholds for number of such regions.

28. (Previously presented) A computer software product according to Claim 27 wherein the computer readable instructions ~~to~~ provide for implementing the step of selecting grown image regions by also using thresholds for ratio of image region luminance to background luminance and area difference between areas derived by growing each image region with multiple thresholds.

29. (Previously presented) A computer software product according to Claim 28 wherein the thresholds for image region area, compactness, width/height ratio, luminance and area difference are: 355 pixels < area < 1700 pixels, 0.17 < compactness < 0.77, width/height ratio < 2.7, luminance percentage < 44%, area difference < 23area/100.

30. (Previously presented) A computer software product according to Claim 27 wherein the computer readable instructions ~~to~~ provide for implementing the step of counting selected grown image regions as actually indicating mitotic figures using also thresholds for region area and luminance.

31. (Currently amended) A computer software product comprising a computer readable medium encoded with computer readable instructions for use in measuring mitotic activity from histopathological specimen <u>color</u> image data obtained from a histopathological specimen stained with a staining agent to <u>color and</u> delineate tissue and cellular structure appropriately for assessment of mitotic activity, the computer readable instructions being for controlling computer apparatus to implement the steps of:

    a)   measuring an intensity profile of an image region <u>in the color image data, the image region</u> corresponding to a potentially mitotic figure, ~~and~~

    b)   counting the image region as indicating a mitotic figure if its <u>intensity</u> profile has a ~~value~~ <u>non-zero number of pixels with intensity associated with mitotic figure imagery, and that pixel number is</u> greater than a prearranged threshold <u>value,</u> ~~at a position in the profile having intensity~~

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~~associated with mitotic figure imagery.~~

   c)   if one or more other image regions corresponding to potentially mitotic figures are available in the specimen image, repeating steps a) and b) for such region or regions,

   d)   repeating steps a), b) and c) for additional histopathological specimen image data in order to obtain mitotic figure counts for a plurality of specimen images, and

   e)   summing the mitotic figure counts obtained in steps a) to d) to provide an indication of degree of mitotic activity.

32.   (Previously presented) A computer software product comprising a computer readable medium encoded with computer readable instructions and for use in measuring mitotic activity from histopathological specimen image data, the computer readable instructions being for controlling computer apparatus to implement the steps of:

   a)   measuring an intensity profile of an image region corresponding to a potentially mitotic figure, and

   b)   counting the image region as indicating a mitotic figure if its profile has a first value not greater than the prearranged threshold at a position in the profile having intensity associated with mitotic figure imagery, a second value greater than a prearranged second threshold, a third value greater than a prearranged third threshold, and a minimum value less than a prearranged fourth threshold.

33.   (Previously presented) A computer software product according to Claim 32 wherein the first value is at one end of the profile, the first and second values adjoin one another in the profile and the third value does not adjoin the second value.

34.   (Previously presented) A computer software product according to Claim 32 wherein the computer readable instructions provide for step a) to include

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preprocessing image data by:

i)   decomposing the image data into overlapping sub-images,

ii)   applying PCA to the sub-images to derive a first Principal Component image,

iii)   thresholding the first Principal Component image to produce a binary image of blobs and background

iv)   rejecting blobs adjacent to or intersecting sub-image boundaries,

v)   filling holes in blobs,

vi)   rejecting blobs too small to correspond to potential mitotic figures, **and**

vii)   reassembling the sub-images into a single image for image region profile measurement as aforesaid in step a).